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Review

Management of Asymptomatic Bacteriuria, Urinary Catheters and Symptomatic Urinary Tract Infections in Patients Undergoing Surgery for Joint Replacement: A Position Paper of the Expert Group 'Infection' of *swissorthopaedics*

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Abstract

In this position paper, we review definitions related to this subject and the corresponding literature. Our recommendations include the following statements. Asymptomatic bacteriuria, asymptomatic leukocyturia, urine discolouration, odd smell or positive nitrite sediments are not an indication for antimicrobial treatment. Antimicrobial treatment of asymptomatic bacteriuria does not prevent periprosthetic joint infection, but is associated with adverse events, costs and antibiotic resistance development. Urine analyses or urine cultures in asymptomatic patients undergoing orthopaedic implants should be avoided. Indwelling urinary catheters are the most frequent reason for healthcare-associated urinary tract infections and should be avoided or removed as soon as possible.

Key words: Asymptomatic bacteriuria, asymptomatic leukocyturia, urine discolouration

Introduction

Periprosthetic joint infection (PJI) is a serious complication after arthroplasty. The relationship between abnormal results in urine analysis and potential risk for PJI often raises questions about the optimal management in patients undergoing surgery for joint replacement

In this position paper, we review definitions related to this subject and the corresponding literature. These recommendations reflect the opinions of the expert group 'Infection' of *swissorthopaedics*, the Swiss Society of Orthopaedics and Traumatology (http://www.swissorthopaedics.ch).

Definitions

Before reviewing the relation between abnormal urinary results and the risk for PJI, commonly used terms should be defined. The definitions of

bacteriuria, pyuria, leukocyturia, asymptomatic bacteriuria (ASB) and symptomatic lower urinary tract infection (UTI) are presented in **table 1** (1, 2). The method of obtaining the urine specimen matters for the definition of ASB. If the methods of obtaining urine samples are not consistent, it suggests an accuracy problem for this variable when comparing studies. Details of urinary sampling methods, the subject of complicated UTI, antibiotic treatment of symptomatic UTI, and pyelonephritis are discussed elsewhere (3), and are beyond the scope of this document. The 2014 recommendations of the Swiss Society for Infectious Diseases regarding the treatment of UTI are available on the society's website (1).

Leukocyturia/pyuria

The differentiation between 'leukocyturia' and 'pyuria' is not common in clinical practice (**table 1**). In this document, we prefer to use the term 'leukocyturia'. It is frequently found in ASB and in other conditions associated with inflammation of the genitourinary tact (2, 4). The presence alone, or in association with nitrite positive sediments or dark-coloured urine is not reason enough to perform a urine culture or to treat an asymptomatic patient with a positive urine culture result. In other words, leukocyturia indicates an inflammation in the genitourinary tract but not necessarily an infection (low positive predictive value). In contrast, absence of leukocyturia does not rule out urinary tract infection (4-6).

Asymptomatic bacteriuria is common

ASB is very common. Its reported prevalence is higher in older persons, in women, and in the presence of genitourinary abnormalities (2, 7). The prevalence of ASB in a general hospital population on the day of admission was recently reported to be 8.5% (8). In diabetic adults and community-dwelling elderly adults, rates of up to 50% or more, have been published (reviewed in (9)). In patients with a chronic indwelling urinary catheter, the rate of ASB is even higher (e.g., up to 100%, reviewed in (10)(11)).

Treatment of ASB in patients undergoing surgery for joint replacement

In previous decades, various orthopaedic centres reported their practice of antimicrobial treatment for preoperatively detected ASB. In these centres, no postoperative haematogenous seeding of bacteria to the artificial joint was observed (12-14). This finding led to the rationale to screen urine preoperatively and, upon detection of bacterial growth, to treat ASB with antibiotics in patients who were undergoing surgery for joint replacement (15, 16). In addition, surgical intervention was often delayed or, alternatively, an 8- to 10-day postoperative course of oral antibiotics was recommended (16, 17). From today's perspective and in our view, this rational is not correct, as outlined with following data.

In 1987, a prospective study on 227 patients undergoing hip or knee replacement found no correlation between PJI and urinary tract infection (18). In 2009, Koulouvaris *et al.* examined the medical records of 19'735 patients (19). The authors found no association between preoperative or postoperative UTI and surgical site infection. The power of the study was low, mainly because the PJI rate was low (0.29%). Nonetheless, this points towards a very low risk of haematogenous seeding of microorganism from the urinary tract to the newly implanted artificial joint. This statement is supported by results from Uçkay *et al.* (11). In their retrospective study, the cumulative duration of estimated urinary tract bacterial colonization for 6'101 total joint arthroplasties patients was approximately 120'000 patient-days (median duration 295 days). In this patient population no immediate haematogenous seeding from the urinary tract to the newly implant was observed (11).

After 2013, studies performed in Spain (20, 21), in Switzerland (22), and a multinational collaboration study (Portugal, Spain, United Kingdom) (23) questioned the benefit of treating ASB. These studies included 215 (21), 471 (20), 510 (22) and 2497 (23) patients, respectively, and the results of these investigations were similar. First, in the few PJIs that occurred postoperatively, the organism that caused the infection was different from that cultured in the preoperatively obtained urine. Second, antimicrobial treatment of ASB did not effectively result in a sterile postoperative urine culture but in change of cultured organisms. For example in the Swiss study, perioperative prophylaxis with cefuroxime changed the culture results from Gram-negative to Gram-positive organisms in 50% of asymptomatic patients (22). Third, lack of antibiotic treatment for ASB was not associated with a higher risk of postoperative PJI due to a microorganism previously found in the urine or a higher risk of postoperative symptomatic UTI. These findings are in line with results from large meta-analyses showing no differences between antibiotic treatment and no treatment of ASB for the development of symptomatic UTI (24).

Table 1. Definitions for terms used to describe abnormal findings in urine analysis.

Term	Description	Definition	Details
Bacteriuria	Presence of bacteria in urine; density is expressed as colony forming units (cfu) organism per millilitre (mL)	Presence or absence of symptoms must be determined	Variables for the definition: method of sampling number of specimens cfu organism /mL gender
Asymptomatic bacteriuria	Isolation of a specified quantitative count of bacteria in an appropriately collected urine specimen obtained from a person without symptoms or signs referable to urinary infection	$\geq 10^5$ cfu of the same organism/mL in 2 consecutive clean voided urine specimens (midstream) for women, or 1 specimen (midstream) for men	If urine is obtained via catheterization, definition includes $\geq 10^2$ cfu organism/mL in 1 specimen. In persons with indwelling urinary catheter, $\geq 10^3$ cfu organism/mL in 1 specimen.
Pyuria	Presence of increased numbers of PMN* leukocytes in urine	No uniformly accepted definition (e.g., $\geq 10^3$ WBC*/mL in non-centrifuged urine). Often referred to as marked leukocyturia	Terms pyuria and leukocyturia often used interchangeably
Leukocyturia	Presence of (undifferentiated) leukocytes in urine	≥10 leukocytes per microscopic field or positive leukocyte esterase result in a reagent strip test	The cut-off (number of leukocytes per microscopic field) can vary between laboratories
Acute uncomplicated urinary tract infection in women	A symptomatic bladder infection characterized by frequency, urgency, dysuria or suprapubic pain in a woman with a normal urinary tract	$\geq 10^2$ cfu/mL organism in voided urine or via catheterization obtained in urine from 1 specimen. In persons with indwelling urinary catheter, $\geq 10^3$ cfu organism/mL in 1 specimen.	Absence of pain and tenderness in the costovertebral angle, no fever, no bacteraemia, no functional or structural abnormalities of the genitourinary tract

* PMN, polymorphonuclear; WBC, white blood cells

The data indicates, however, that the presence of ASB prior to surgery has no clinical relevance, and therefore, should neither indicate preoperative antimicrobial treatment, nor delay surgery, nor lead to prescription of postoperative antibiotics. Also, routine perioperative antibiotic prophylaxis should not be switched to a compound active against microorganisms found in the urine of patients with ASB. Cordero-Ampuero *et al.* (20) randomly assigned patients undergoing surgery for total hip arthroplasty or hemiarthroplasty and with ASB to receive specific antibiotics (n = 117) or routine antibiotic prophylaxis (n = 126). Thirteen patients developed PJI after 3 months. Bacteria cultured from the wound were not those cultured in urine samples in any case, irrespective of the previous choice of antimicrobial compound.

In the work by Sousa *et al.* (23), the presence of ASB was associated with a higher risk for PJI, irrespective of organisms found in the urine. In our view, the interpretation of this finding falls into the category of weighting patients' comorbidities for postoperative complications, including infections. In other words, a wide range of patient-related factors increases the risk of surgical site infections (25, 26). Sousa et al. (23) and the accompanying editorial note by Duncan (27) suggested that ASB may also be a surrogate marker for increased risk of infection, but not a risk factor itself. In other words, the study suggests an epidemiological association but not a causal relation between ASB and development of a PJI of a non-urinary origin (28).

Many of the cited studies face the criticism of being underpowered. Indeed, Bouvet *et al.* (22) calculated a sample size of 2 x 50'979 arthroplasties for a superiority trial (α 0.05, power 80%, difference in infection risk 0.15%) and approximately 2 x 200'000 for a non-inferiority trial. It is not realistic that such a trial will ever be performed. However, Bouvet *et al.* (22) evaluated the costs associated with the screening and treatment for ASB (Geneva, Switzerland). On the basis of 510 elective arthroplasties performed in one year, the estimated minimal laboratory costs for preoperative urinary analyses were 25'000 Swiss Francs. The estimated savings by withholding antibiotics for ASB were at least 2'000 Swiss Francs (22). Understandably, this cost estimate will be likely higher when ASB with multi-drug-resistant bacteria are treated.

The power calculation is also important to highlight collateral damages caused by unnecessary use of antibiotics. Antibiotic treatment for ASB is associated with significantly more adverse events and the development of resistance (24, 29). Unfortunately, ASB has become a major cause of inappropriate antimicrobial use (30, 31). This reasoning coincides with epidemiological data showing that the rate of ASB is higher in older persons and in the presence of genitourinary abnormalities (2, 32). Evidently, these patient groups overlap with those requiring arthroplasty for osteoarthritis.

Based on these arguments, we do not recommend urine analyses in asymptomatic patients undergoing surgery for orthopaedic implants. Our recommendation is valid for all asymptomatic patients regardless of gender, age, local urologic cancer or chronic urinary catheter use. We also support this recommendation for patients treated with immunosuppressive compounds, although few data on PJI are available for this patient population.

The rational for this recommendation is based on the observation of similar low PJI rates due to Gram-negative rods or enterococci (i.e., microorganisms typically found in the urine) in the general population (33, 34) and in a nested survey within the Swiss Transplant Cohort Study (*Ilker Uçkay, Andrey Diego, unpublished data*). Similarly, Vergidis *et al.* (35) retrospectively reviewed the arthroplasty cohort of the Mayo Clinic. Among 367 solid organ transplant patients, 12 PJIs were identified. Eight of them were caused by staphylococci and streptococci, two by nontuberculous mycobacteria, and two cases were culture-negative. Only one co-infection with *Klebsiella* spp. (0.27%) among all transplant patients was found.

If a urinary culture is nonetheless performed, a positive result should not be treated in asymptomatic patients. The routine perioperative antibiotic prophylaxis should not be modified. Moreover, the results, including the presence of leukocyturia, urine decolouration, odd smell or positive nitrite sediments should not lead to postponement of the surgical intervention (36).

Symptomatic bacteriuria/urinary tract infection

The diagnosis and treatment of UTIs is discussed elsewhere (37, 38). Guideline recommendations for the treatment of UTI vary between countries and institutions on the basis of local resistance epidemiology and results from surveillance systems. The 2014 recommendations of the Swiss Society for Infectious Diseases regarding the treatment of UTI are available on the society's website (1). The decision to perform surgery after a UTI has been identified preoperatively depends on the extent of infection and the timing of surgery. In patients with signs of sepsis (e.g., urosepsis or positive blood cultures), a delay of surgery is recommended until the infection is controlled. Such a recommendation is, however, less clear for uncomplicated cystitis without sepsis. In our view, it is not necessary to postpone surgery, though antimicrobial treatment for UTI must be initiated promptly. The scientific rational for this opinion statement however remains to be elaborated. In these cases, treatment recommendations do not differ from those for UTI in other patients (1). This is also true for postoperative UTI.

Prevention of postoperative urinary tract infection

There are conflicting results about whether postoperative UTI is a risk factor for PJI. While several studies have suggested that postoperative UTI is indeed a risk factor for PJI (26, 39), a recent review and meta-analysis did not confirm this hypothesis (40). Because the precise definitions of UTIs in these large data analyses are frequently missing, the interpretation of the results becomes ambiguous. Nonetheless, healthcare-associated infection, including symptomatic UTI after joint replacement, must be avoided.

The presence of a urinary catheter is the most important risk factor for healthcare-associated UTI (41). Indwelling urinary catheters in place for ≥2 days result in a significant increase in nosocomial infections (42). Thus, infection control strategies to prevent UTI are pivotal for every orthopaedic centre. Stéphan *et al.* (43) demonstrated that multifaceted interventions after orthopaedic surgery led to a reduction in the number of UTIs to two-thirds of that in the control group. These interventions included restricting urinary catheterization to a defined patient group, inserting catheters by using aseptic techniques and sterile equipment, connecting catheters to a closed drainage system, and removing the urinary catheter (if insertion was necessary at all) before patient discharge from the postanaesthesia care unit (43). In addition, specifically tailored, locally developed guidelines were distributed; educational sessions were performed; and posters with a visual display of the guidelines were hung up. Guidelines were applied in the operating room, postanaesthesia care unit and surgical ward (43). These combined efforts demonstrate the multidisciplinary need to implement prevention strategies. It is important to maintain a suitable educational level in order to sustain the high success rate of such interventions (44). This level can be achieved by engaging local leaders or a multidisciplinary team who are in decision-making positions (44).

Conclusions

For ASB, a paradigm shift from treatment to non-treatment has occurred in recent years. Treating ASB does more harm than good and should be avoided. In addition, the presence of ASB should not postpone surgery. Perioperative antibiotic prophylaxis should not be modified because of ASB. This recommendation is equally valid for the presence of asymptomatic leukocyturia or positive nitrite sediments.

The most common risk factors for postoperative healthcare-associated UTIs are indwelling urinary catheters. They should be indicated for only a few patient groups and removed as rapidly as possible. Preventive strategies require a multifaceted approach and constant engagement by all involved parties.

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Competing Interests

The authors have declared that no competing interest exists.

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